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Attenuation of Brain Hyperbaric Oxygen Toxicity of Fasting is not Related to Ketosis

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(MED-02)
Department of the Navy
Washington, DC 20372-5120

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT DISTRIBUTION STATEMENT A: Approved for public release; distribution is unlimited
2b. DECLASSIFICATION/DOWNGRADING AUTHORITY	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION Naval Medical Research Center 6b. OFFICE SYMBOL (If Applicable)	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State, and ZIP Code) 8901 Wisconsin Avenue, Bethesda, Maryland 20889-5607	7b. ADDRESS (City, State, and Zip Code)
8a. NAME OF FUNDING SPONSORING ORGANIZATION 8b. OFFICE SYMBOL (If Applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code)	10. SOURCE OF FUNDING NUMBERS 61152N MR00001.001-1501/637306N M00096.001-1705

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
			DN242100/DN240 578

11. TITLE: ATTENUATION OF BRAIN HYPERBARIC OXYGEN TOXICITY BY FASTING IS NOT RELATED TO KETOSIS

12. PERSONAL AUTHOR(S)
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13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
ARTICLE	FROM _____ TO _____	1999 FEBRUARY	5

16. SUPPLEMENTARY NOTATION
PRINTED IN UNDERSEA AND HYPERBARIC MEDICINE 26(2): 99-103

17. COSATI CODES		
FIELD	GROUP	SUB-GROUP

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
STARVATION, KETOSIS, CONVULSIONS, CENTRAL NERVOUS SYSTEM OXYGEN TOXICITY, GLUCOSE, BRAIN

19. ABSTRACT (Continue on reverse if necessary and identify by block number)
The effect of 24 h of fasting and changes in blood glucose and β-hydroxybutyrate (BHB) level on latency to seizures in hyperbaric oxygen (HBO2) was studied. Conscious, unrestrained rats implanted with cortical electroencephalogram electrodes were exposed to 0.5 Mpa (gauge pressure) 02 until seizures were observed. Fasting for 24 h significantly ($P<0.01$) decreased blood glucose (from 8.6± 0.9 in fed to 6.9± 0.7 mM in the fasted group), increased blood BHB (0.07± 0.02 mM to 0.38± 0.10 mM, respectively), and prolonged the latency to seizures compared with normally fed animals (21.0± 9.8 vs. 34.6± 17.7 min, $P<0.05$). Injection of the ketone precursor 1,3-butanediol(BD) to the fed animals increased blood BHB level to 0.72± 0.32; however, seizure latency remained the same as in fed animals. Restoration of blood glucose in fasted animals to the same level as in the fed group did not reverse the protection achieved by fast; instead it increased the latency to seizures. The results indicate that the protection against HBO2 seizures by fasting in short starvation is not related to the increase in circulating ketone bodies or decrease in blood glucose.

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
[X] UNCLASSIFIED/UNLIMITED [ ] SAME AS RPT. [ ] DTIC USERS	Unclassified

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE (Include Area Code)	22c. OFFICE SYMBOL
NEDU Librarian	850-230-3100	

DD Form 1473

Attenuation of brain hyperbaric oxygen toxicity by fasting is not related to ketosis

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Chavko M, Braisted JC, Harabin AL. Attenuation of brain hyperbaric oxygen toxicity by fasting is not related to ketosis. Undersea Hyper Med 1999; 26(2):99–103.—The effect of 24 h of fasting and changes in blood glucose and β-hydroxybutyrate (BHB) level on latency to seizures in hyperbaric oxygen (HBO_2) was studied. Conscious, unrestrained rats implanted with cortical electroencephalogram electrodes were exposed to 0.5 MPa (gauge pressure) O_2 until seizures were observed. Fasting for 24 h significantly ($P < 0.01$) decreased blood glucose (from 8.6 ± 0.9 in fed to 6.9 ± 0.7 m*M* in the fasted group), increased blood BHB (0.07 ± 0.02 m*M* to 0.38 ± 0.10 m*M*, respectively), and prolonged the latency to seizures compared with normally fed animals (21.0 ± 9.8 vs. 34.6 ± 17.7 min, $P < 0.05$). Injection of the ketone precursor 1,3-butanediol (BD) to the fed animals increased blood BHB level to 0.72 ± 0.32; however, seizure latency remained the same as in fed animals. Restoration of blood glucose in fasted animals to the same level as in the fed group did not reverse the protection achieved by fast; instead it increased the latency to seizures. The results indicate that the protection against HBO_2 seizures by fasting in short starvation is not related to the increase in circulating ketone bodies or decrease in blood glucose.

starvation, ketosis, convulsions, central nervous system oxygen toxicity, glucose, brain

Hyperbaric oxygen (HBO_2) is used in various diving-related situations, as well as in the treatment of carbon monoxide intoxication and in other medical situations (1,2). However, breathing oxygen at high partial pressures may result in the manifestation of central nervous system (CNS) toxicity, including seizures, within a time lag inversely proportional to the O_2 partial pressure. These complications impose major limitations on HBO_2 use in high pressure or for longer exposures, or both (3). The development of pharmacologic or physiologic interventions to decrease the risk of seizures and increase safety would therefore be beneficial, both therapeutically and operationally.

Acute fasting, which results in hypoglycemia and ketosis, provides protection from seizures in humans and animals (4–6). A ketogenic diet, which is high in fat and an alternative to starvation, is effective against some experimental seizures in animals (7–9) and is used to control intractable seizures in children (review in 10). Previous studies also show that moderate fasting increases survival time (11) and seizure latency (12) in HBO_2 exposure. Both fasting and the ketogenic diet induce an increase in plasma ketone bodies [primarily β-hydroxybutyrate (BHB) and acetoacetate], and a decrease in blood glucose. Most likely, the ketosis is the variable responsible for seizure control (5). The mechanism of the protection remains unknown (10). Preferential utilization of ketones, rather than glucose for brain metabolic function, seems fundamental in the anticonvulsant effect of a ketogenic diet, and resumption of a normal diet rapidly reverses the benefit of a ketosis (8).

The objective of this study was to determine if protection from HBO_2 seizures by acute, short fasting is related to the ketosis or to the mild hypoglycemia resulting from this treatment, or to both. For this purpose, blood glucose and ketone levels were manipulated in the fed and fasted rats by injection of glucose or a ketone precursor, 1,3-butanediol (BD), and the latency to seizures was recorded.

METHODS

Animals and O_2 exposures: Rats (male, Sprague–Dawley, pathogen-free, 360–460 g) were anesthetized with ketamine (100 mg · kg^{-1}) and xylazine (5 mg · kg^{-1}), and four stainless steel electrodes were inserted through the skull bilaterally over the posterior and anterior cortex. A miniature connector was joined to the electrodes, which were secured to the skull with dental acrylic. The rats recovered for 6–7 days. Animal weight was monitored daily. On the morning of the exposure, unrestrained animals were placed in a hyperbaric chamber, and permitted to acclimate for several minutes. After acclimation, a baseline electroencephalogram (EEG) was recorded for 5 min (Grass Instrument, Quincey, MA). The chamber was then compressed to 0.5 MPa (gauge pressure) with O_2 at 0.1 MPa · min^{-1}. The chamber was flushed with 100% O_2 for 1.5 min to raise the O_2 level to >99%. During exposure,

inspired CO_2 was monitored and remained below 0.01%. The animal and the EEG were monitored throughout the exposures by a blinded observer unaware of the animal's treatment. When the animal developed a seizure, the chamber was decompressed at 0.1 MPa · min^{-1}.

Treatments: For series 1 (non-injected animals), the animals were divided into two groups. Group 1 (n = 10) received regular rat chow and tap water ad libitum; group 2 (n = 10) was fasted for 24 h with free access to water before exposure. For series 2 (drug- or saline-injected animals), the animals were divided into five groups. Group 1 (fed + saline, n = 12) received regular chow and tap water ad libitum; group 2 (fasted + saline, n = 14) animals were fasted for 24 h with free access to water; group 3 (fed + BD, n = 10) animals were fed and injected with BD (25 mM · kg^{-1}); group 4 (fasted + BD, n = 6) animals were fasted and injected with BD (25 mM · kg^{-1}); and group 5 (fasted + glucose, n = 14) animals were fasted for 24 h and injected with normotonic (277 mOsM) 5% glucose (5 mM · kg^{-1}) to restore plasma glucose to fed levels. All animals in this series received an intraperitoneal injection of saline, BD, or glucose 30 min before O_2 exposure.

Blood biochemical analysis: Blood samples were taken from the tail vein before and 30 min after the animals were given injections. Plasma was separated immediately and frozen for later analysis. The samples were deproteinized by addition of 1 M perchloric acid, and the supernatant was assayed for glucose (13) and BHB level (14).

Data are expressed as mean ± 1 SD and were analyzed using analysis of variance and the Newman-Keuls test.

RESULTS

The EEG seizure that terminated exposure typically lasted about 1 min. It consisted of high-amplitude, high-frequency spikes, followed by depressed EEG and then transformation to polyspikes and wave formation. The animals usually exhibited clonic–tonic movements of the head and upper body during the EEG seizure.

Animals in all fasted groups lost approximately 6% of their pre-fast body weight, whereas controls maintained or slightly increased body weight during the 24-h period preceding the O_2 exposure (Table 1).

In series 1 (non-injected animals), a 24-h fast significantly (P = 0.01) increased latency to seizures from 16.6 ± 5.7 to 26.9 ± 11.4 min. In series 2, fasting resulted in about the same increase in latency to seizure as observed in series 1 (Fig. 1). One saline-injected animal had an unusually long latency of 82 min and was not included in the statistics. This latency is about eight standard deviations from the mean latency of saline-injected animals (21.0 ± 9.8 min) and was determined to be an outlier. Inclusion of this animal caused an increase in group variability sufficient to abolish the significance in seizure latency in group 2.

Injection of BD to the fed animals had no effect on seizure latency compared with saline-injected animals (Fig. 1). BD injected to the fasted animals eliminated the protection of fasting. On the other hand, controlled glucose administration to the fasted animals further increased the latent time to seizure (Fig. 1).

Biochemical variables: During the 24-h fasting period, reciprocal changes in blood glucose and BHB concentrations were found (Table 1). The blood glucose concentration fell and differed significantly ($P < 0.01$) from the fed control, whereas the blood BHB concentration rose and also differed significantly ($P < 0.01$) from the control levels. A significant increase ($P < 0.01$) in plasma BHB levels resulted from BD injection (Table 1). Animals that were fasted and injected with glucose had their glucose restored to levels indistinguishable from the fed group, and significantly increased vs. the fasted group while their BHB concentration was not changed from the fasted group (Table 1).

DISCUSSION

This study shows that a short-term, 24-h fast significantly increases latency to HBO_2-induced seizures. This is in accord with the anticonvulsant effect of fasting in human epilepsy (4) and in experimental seizures induced by sound (6) or electroshock (5). Recently, Bitterman et al. (12) reported a significant delay in seizure latency during exposure to 5 atm after a 36-h fast, and a slight but non-significant increase after 24 h of starvation.

It is presumed that the anticonvulsant effect of both a ketogenic diet and fasting is related to the ketosis, and a shift in brain metabolism to the use of ketones instead of glucose. Experimental data, however, do not fully support a direct relationship between ketone level and anticonvulsant effect, and the precise mechanism by which ketosis protects against seizures remains to be identified (10).

Our data show that 24 h of fasting significantly increased blood BHB and decreased glucose. It should be considered, therefore, whether the ketosis or the decreased plasma glucose level is responsible for the delay in seizure latency demonstrated in fasted animals. If ketosis were the basis for the effect of fasting, infusion of ketones would provide protection to normally fed animals. For induction of ketosis, we have used i.p. injection of BD, a synthetic ethanol dimer, which is metabolized in the liver to BHB and acetoacetate (15). It has been shown that BD induces cerebral protection in models of hypoxia and ischemia (16,17), probably by elevating blood ketones, which can be used as an alternate substrate instead of glucose for brain

Table 1: Changes in Body Weight, Blood Glucose, and BHB Levels in Saline and Drug-Treated Animals[a]

		Glucose, m*M*		BHB, m*M*	
Treatment	Δ Body Weight, g	Before Injection	After Injection	Before Injection	After Injection
Fed + saline	1.0 ± 0.7	7.73 ± 0.85	8.63 ± 0.93	0.06 ± 0.02	0.07 ± 0.02
Fast + saline	−25.0 ± 4.4[b]	5.97 ± 0.82[c]	6.91 ± 0.71[c]	0.41 ± 0.11[c]	0.38 ± 0.10[c]
Fed + BD	3.0 ± 2.5	ND	8.50 ± 1.31[d]	ND	0.72 ± 0.32[c,d]
Fast + BD	−27.0 ± 5.3[b]	6.28 ± 0.75[c]	7.41 ± 0.75	0.40 ± 0.11[c]	0.88 ± 0.11[c,d]
Fast + glucose	−27.0 ± 5.3[b]	5.94 ± 0.81[c]	8.27 ± 1.23[d]	0.40 ± 0.10[c]	0.35 ± 0.10[c]

[a]Values are mean ± SD; ND = not determined. [b]$P < 0.01$ vs. fed + saline and fed + BD groups; [c]$P < 0.01$ vs. fed + saline group; [d]$P < 0.01$ vs. fast + saline group (Newman-Keuls test).

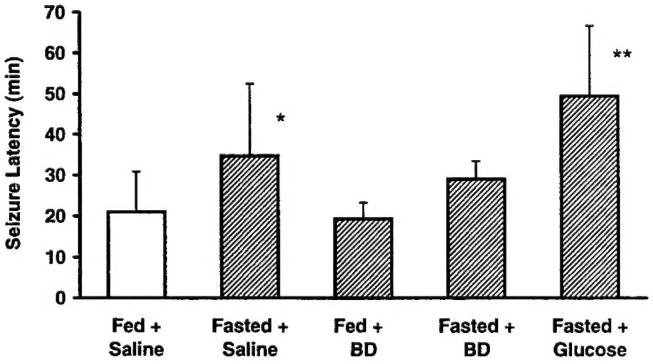

FIG. 1—Seizure latency (±SD) in the saline- and drug-treated animals (series 2). *$P < 0.05$ compared with the fed and saline and fed and BD group; **$P < 0.05$ compared with all other groups (Newman– Keuls test).

metabolism. In our BD-treated group, BHB blood concentration was 0.72 ± 0.32 m*M*, which is almost twice that after a 24-h fast. However, this increase did not change seizure latency compared with saline-injected controls. The data therefore refute an assumption that fasting provides protection against HBO_2 seizures solely by elevating blood ketone level.

On the other hand, it seemed reasonable that ketosis might be effective in combination with some other factor(s) also activated by fasting. For this reason, BD was also administered to the group of animals after a 24-h fast. This treatment, like BD administration to the fed animals, had no significant effect of seizure latency compared with saline-injected animals. In fact, injecting BD into fasting animals seems to eliminate the protective effect of starvation observed with a 24-h fast. This finding is consistent with the observation that BD-treated rats demonstrated post-ischemic seizures earlier than saline-treated animals (18).

The second set of experiments was focused on the role of decreased blood glucose observed after fasting. It has been shown that the anticonvulsant effect of the ketogenic diet against seizures can be reversed quickly with resumption of a normal diet both in mice and in humans (8,19). Ketosis does not seem to affect the relation between glucose phosphorylation and O_2 consumption in awake, resting rats; however it is not known if this relationship is maintained when glucose utilization is stimulated. Torbati et al. (20) have demonstrated that glucose utilization increases during exposure to 5 atm O_2 long before seizures. It can therefore be supposed that ketones might contribute more significantly to the higher energy demands when metabolism is stimulated. In that case, glucose supplementation should reverse the protective effect of increased ketones. Therefore, in one group of animals we administered glucose to fasted animals to reach exactly the same levels as in the fed animals. This manipulation did not reverse the effect of starvation, instead seizure latency was even longer than seen after a 24-h fast. This finding seems to correlate with the observation that the injection of glucose in normally fed rats induced protection against HBO_2 seizures, whereas insulin aggravated HBO_2 brain toxicity (21). The absence of an effect of BD animals on seizure latency in both saline-injected and fasted does not support the idea that starvation protects against HBO_2 seizures via a metabolic shift in the brain to utilize ketones instead of glucose.

Protection against free radical damage in lipid and proteins might explain how the fast increases tolerance to HBO_2. One study demonstrated that an overnight food restriction was sufficient to decrease ethane production (an index of lipid peroxidation) during exposure to 100% O_2, although there was no effect during air exposure (22).

It has been demonstrated that food deprivation affects expression of many genes, which can also be related to the delay in seizure latency in HBO_2 exposure. For instance, a 48-h fast significantly reduced nitric oxide synthase (NOS) transcription in the rat hypothalamus (23). Whether this regionally specific decrease in NOS is related to the protection against O_2 seizures is not known. However, systemic administration of NOS inhibitors that depress NOS activity in the whole brain, significantly increased

latency to seizures in rats (24,25). Nitric oxide may influence seizure latency in HBO_2 exposures in several ways: by oxidative damage, through formation of peroxynitrite and hydroxyl radicals (26), or by its potent vasodilatory effect (25). It would be interesting to know how changes in NOS activity in specific brain regions will affect sensitivity to HBO_2. A further possibility is that the protection against HBO_2 toxicity is secondary to the fasting-induced changes in the hypothalamo-pituitary adrenal axis (27). It has been reported that exposure of normal rats to HBO_2 results in an activation of the sympathetic adrenomedullary system indicated by a progressively elevated blood adrenaline, noradrenaline (28), and glucose concentration (29). This activation seems to attenuate HBO_2 brain toxicity, as adrenalectomy (30) and beta adrenergic blockers (31) delay time to seizures. Food deprivation might protect by the same mechanism as it suppresses stress-induced rise in catabolic hormones (32).

Our results confirm a recent report that mild starvation protects against seizures induced by HBO_2 exposures. Apparently, this effect cannot be explained by ketosis or decreased blood glucose levels, which are changed in opposite ways during the fast. Other factors, such as a decrease in oxidative damage by fasting, may provide an alternative for this protection. Whatever the mechanism of protection against HBO_2 seizures by food deprivation, it might be useful in increasing protection against CNS O_2 toxicity in common situations such as diving or HBO_2 therapy.

This work was supported by NMRDC Work Unit Nos. 61152N MR00001.001-1501 and 637306N M00096.001-1705. The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

The experiments reported herein were conducted according to the principles set forth in the *Guide for the Care and Use of Laboratory Animals*, Institute of Laboratory Animal Resources, National Research Council, National Academy Press, 1996.

The authors thank Ms. T. Cope and Ms. N. J. Outsa for technical assistance and Ms. S. Mannix and Ms. D. Temple for editorial assistance.

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REFERENCES

1. Melamed Y, Shupak A, Bitterman H. Medical problems associated with underwater diving. N Engl J Med 1992; 26:30–35.
2. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. N Engl J Med 1996; 34:1642–1648.
3. Lambertsen CJ. Effects of oxygen at high partial pressure. In: Fenn WO, Rahn H, eds. Handbook of physiology: respiration, vol II. Washington, DC: American Physiological Society, 1965:1027–1046.
4. Peterman MG. Epilepsy in childhood. JAMA 1948; 138:1012–1018.
5. DeVivo DC, Malas KL, Lackie MP. Starvation and seizures. Observations on the electroconvulsive threshold and cerebral metabolism of the starved adult rat. Arch Neurol 1975; 32: 755–760.
6. Mahoney AW, Hendricks DG, Bernhard N, Sisson DV. Fasting and ketogenic diet effects on audiogenic seizure susceptibility of magnesium deficient rats. Pharmacol Biochem Behav 1983; 18: 683–687.
7. Millichap JG, Jones JD, Rudis BR. Mechanism of anticonvulsant action of ketogenic diet. Am J Dis Child 1964; 107:593–604.
8. Uhlemann ER, Neims AH. Anticonvulsant properties of the ketogenic diet in mice. J Pharmacol Exp Ther 1972; 80:231–238.
9. Appleton DB, DeVivo DC. An animal model for the ketogenic diet. Electroconvulsive threshold and biochemical alterations consequent upon a high-fat diet. Epilepsia 1974; 15:211–227.
10. Prasad AN, Stafstrom CF, Holmes GL. Alternative epilepsy therapies: the ketogenic diet, immunoglobulins, and steroids. Epilepsia 1996; 37(suppl 1):S81–S95.
11. Campbell JA. Oxygen poisoning and tumor growth. Br J Exp Pathol 1937; 18:191–197.
12. Bitterman N, Skapa E, Gutterman A. Starvation and dehydration attenuates CNS oxygen toxicity in rats. Brain Res 1997; 761:146–150.
13. Carroll JJ, Smith N, Babson AL. A calorimetric serum glucose determination using hexokinase and glucose-6-phosphate dehydrogenase. Biochem Med 1970; 4:171–176.
14. Williamson DH, Mellanby J, Krebs HLA. Enzymic determination of D(-)-β-hydroxybutyric acid and acetoacetic acid in blood. Biochem J 1962; 82:90–95.
15. Tate RL, Mehlman MA, Tobin RB. Metabolic fate of 1,3-butanediol in the rat: conversion to β-hydroxybutyrate. J Nutr 1971; 101:1719–1726.
16. Kirsch JR, D'Alecy LG, Mongroo PB. Butanediol induced ketosis increases tolerance to hypoxia in the mouse. Stroke 1980; 11: 506–513.
17. Marie C, Bralet A-M, Bralet J. Protective action of 1,3-butanediol in cerebral ischemia. A neurologic, histologic, and metabolic study. J Cereb Blood Flow Metab 1987; 7:794–800.
18. Lundgren J, Smith M-J, Mans AM, Siesjo BK. Ischemic brain damage is not ameliorated by 1,3-butanediol in hyperglycemic rats. Stroke 1992; 23:719–724.
19. Huttlenlocher PR. Ketonemia and seizures: metabolic and anticonvulsant effects of two ketogenic diets in childhood epilepsy. Pediatr Res 1976; 10:536–540.
20. Torbati D, Greenberg J, Lambertsen CJ. Correlation of brain glucose utilization and cortical electrical activity during development of brain oxygen toxicity. Brain Res 1983; 262:267–273.
21. Beckman DL, Crittenden DJ, Overton DH, Blumenthal SJ. Influence of blood glucose on convulsive seizures from hyperbaric oxygen. Life Sci 1982; 31:45–49.
22. Habib MP, Dickerson F, Moradian AD. Ethane production rate in vivo is reduced with dietary restriction. J Appl Physiol 1990; 68:2588–2590.
23. Ueta Y, Levy A, Chowdrey HS, Lightman SL. Inhibition of hypothalamic nitric oxide synthase gene expression in the rat paraventricular nucleus by food deprivation is independent of serotonin depletion. J Neuroendocrinol 1995; 7:861–865.
24. Zhang J, Su Y, Oury TD, Piantadosi CA. Cerebral amino acids, norepinephrine and nitric oxide metabolism in CNS oxygen

toxicity. Brain Res 1993; 606:56–62.
25. Chavko M, Braisted JC, Outsa NJ, Harabin AL. Role of cerebral blood flow in seizures from hyperbaric oxygen exposure. Brain Res 1998; 791:75–82.
26. Beckman JS, Beckman TW, Chen J, Marshall PA, Freeman BA. Apparent hydroxyl radical production by peroxynitrite: implications for endothelial injury from nitric oxide and superoxide. Proc Natl Acad Sci USA 1990; 87:1620–1624.
27. Jung RT, Shetty PS, James WPT. Nutritional effects on thyroid arid catecholamine metabolism. Clin Sci 1980; 58:183–191.
28. Cross MH, Houlihan RT. Sympathoadrenomedullary response of the rat to high oxygen pressures. J. Appl Physiol 1969; 27:523–527.
29. Torbati D, Torbati A. Blood glucose as a predictive measure for central nervous system oxygen toxicity in conscious rats. Undersea Biomed Res 1986; 13:147–154.
30. Singh AK, Bannister FW, Effect of adrenalectomy on convulsions induced by high-pressure oxygen. Can J Physiol Pharmacol 1979; 57:688–694.
31. Torbati D. Effect of propranolol on brain electrical activity during hyperbaric oxygenation in the rat. Undersea Biomed Res 1985; 12:423–429.
32. Wronska D, Niezgoda J, Sechman A, Bobek S. Food deprivation suppresses stress-induced rise in catabolic hormones with a concomitant tendency to potentiate the increment of blood glucose. Physiol Behav 1990; 48:531–537.